

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

These amendments introduce no new matter and support for the amendment is replete throughout the specification and claims as originally filed. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter, or agreement with any objection or rejection of record.

Listing of Claims:

1. -102. (Canceled)

103. (Original) A composition comprising a caged RNA, the caged RNA comprising:

an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; and,

one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in a cell comprising the caged RNA.

104. (Original) A composition comprising a caged RNA, the caged RNA comprising:

an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA; and,

one or more first caging groups associated with the RNA, the first caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in a cell comprising the caged RNA.

105. (Original) The composition of claim **103** or **104**, wherein the first caging groups inhibit the RNA from initiating RNA interference of the target mRNA by at least about 30%, at least about 50%, at least about 75%, at least about 90%, at least about 95%, or at least about 98%, as compared to the RNA in the absence of the first caging groups.

106. (Original) The composition of claim **103** or **104**, wherein the first caging groups prevent the RNA from initiating RNA interference of the target mRNA.

107. (Original) The composition of claim **103** or **104**, wherein removal of or an induced conformational change in the first caging groups permits the RNA to initiate RNA interference of the target mRNA.

108. (Original) The composition of claim **103**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand.

109. (Original) The composition of claim **108**, wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs.

110. (Original) The composition of claim **109**, wherein the first polyribonucleotide and the second polyribonucleotide each comprise a two nucleotide TT 3' overhang, or wherein the first polyribonucleotide and the second polyribonucleotide form a duplex over their entire length.

111. (Original) The composition of claim **109**, wherein at least one of the one or more first caging groups is covalently attached to a 5' hydroxyl or a 5' phosphate of the second polyribonucleotide.

112. (Original) The composition of claim **103**, wherein the RNA comprises a self-complementary polyribonucleotide.

113. (Original) The composition of claim **103**, wherein the double-stranded region comprises fewer than about 25 base pairs, fewer than about 30 base pairs, fewer than about 50 base pairs, fewer than about 80 base pairs, fewer than about 150 base pairs, fewer than about 250 base pairs, fewer than about 500 base pairs, fewer than about 1000 base pairs, or fewer than about 1500 base pairs.

114. (Original) The composition of claim **104**, wherein the polyribonucleotide strand comprises between 10 and 100 nucleotides, between 10 and 80 nucleotides, between 10 and

50 nucleotides, between 10 and 30 nucleotides, between 15 and 30 nucleotides, or between 19 and 25 nucleotides.

115. (Original) The composition of claim 104, wherein at least one of the one or more first caging groups is covalently attached to a 5' hydroxyl or a 5' phosphate of the polyribonucleotide.

116. (Original) The composition of claim 103 or 104, comprising the target mRNA, a cell, a cell comprising the target mRNA, or a cell comprising the caged RNA.

117. (Original) The composition of claim 103 or 104, wherein the one or more first caging groups associated with the RNA are covalently attached to the RNA.

118. (Original) The composition of claim 103, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein the first caging group is covalently attached to the first polyribonucleotide and to the second polyribonucleotide.

119. (Original) The composition of claim 118, wherein the first caging group is attached to the 3' end of the first polyribonucleotide and to the 5' end of the second polyribonucleotide.

120. (Original) The composition of claim 103 or 104, wherein the one or more first caging groups are removable by sonication, photoactivatable, or photolabile.

121. (Original) The composition of claim 103 or 104, wherein the one or more first caging groups each comprises a first binding moiety; the composition comprising a second binding moiety that can bind at least one of the first binding moieties.

122. (Original) The composition of claim 103, wherein the RNA comprises at least one label, wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label.

123. (Original) The composition of claim 122, wherein the label is a fluorescent label, and wherein the initiation-dependent change in the signal output of the label is a change in fluorescent emission.

124. (Original) The composition of claim **123**, wherein the labeled RNA comprises at least one quencher, wherein the label and the quencher are positioned in the RNA such that fluorescent emission by the label is quenched by the quencher, wherein initiation of RNA interference by the labeled RNA results in unquenching of the label, and wherein the initiation-dependent change in the signal output is an increase in the fluorescent emission by the label.

125. (Original) The composition of claim **124**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand; wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs; and wherein the label is attached to the first polyribonucleotide and the quencher is attached to the second polyribonucleotide, or the label is attached to the second polyribonucleotide and the quencher is attached to the first polyribonucleotide.

126. (Original) The composition of claim **125**, wherein:

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the label and the quencher is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the

other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the label and the quencher is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the label and the quencher is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the label is attached at the 3' end of the first polyribonucleotide and the quencher is attached at the 3' end of the second polyribonucleotide;

the quencher is attached at the 3' end of the first polyribonucleotide and the label is attached at the 3' end of the second polyribonucleotide; or,

one of the label and the quencher is attached at the 5' end of the first polyribonucleotide and the other of the label and the quencher is attached at the 3' end of the second polyribonucleotide.

127. (Original) The composition of claim **123**, wherein the labeled RNA comprises two fluorescent labels, one being a donor and the other being an acceptor; wherein the donor and acceptor are positioned within the RNA such that energy transfer occurs between them; wherein initiation of RNA interference by the labeled RNA results in loss of energy transfer between the donor and the acceptor; and wherein the initiation-dependent change in the signal output is a decrease in fluorescent emission by the acceptor following excitation of the donor.

128. (Original) The composition of claim **127**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand; wherein the first polyribonucleotide comprises between 19 and 25 nucleotides, the second polyribonucleotide comprises between 19 and 25 nucleotides, and the double-stranded region comprises between 19 and 25 base pairs; and wherein the donor is attached to the first polyribonucleotide and the acceptor is attached to the second polyribonucleotide, or the donor is attached to the second polyribonucleotide and the acceptor is attached to the first polyribonucleotide.

129. (Original) The composition of claim **128**, wherein:

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 3' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is located within three nucleotides of the 5' end of the second polyribonucleotide;

one of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the first polyribonucleotide, and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the second polyribonucleotide;

one of the donor and the acceptor is located within three nucleotides of the 5' end or the 3' end of the first or second polyribonucleotide and the other of the donor and the acceptor is located more than three nucleotides from the 5' end and more than three nucleotides from the 3' end of the opposite polyribonucleotide;

the donor is attached at the 3' end of the first polyribonucleotide and the acceptor is attached at the 3' end of the second polyribonucleotide;

wherein the acceptor is attached at the 3' end of the first polyribonucleotide and the donor is attached at the 3' end of the second polyribonucleotide; or,

one of the donor and the acceptor is attached at the 5' end of the first polyribonucleotide and the other of the donor and the acceptor is attached at the 3' end of the second polyribonucleotide.

130. (Original) The composition of claim **104**, wherein the RNA comprises at least one label, wherein initiation of RNA interference of the target mRNA by the labeled RNA in the cell results in an initiation-dependent change in a signal output of the label.

131. (Original) The composition of claim **103** or **104**, wherein the RNA is associated with a cellular delivery module that can mediate introduction of the RNA into a cell.

132. (Original) The composition of claim **131**, wherein the cellular delivery module comprises a polypeptide, a PEP-1 peptide, an amphipathic peptide, an MPG□NLS peptide, a cationic peptide, a homopolymer of D-arginine, a homopolymer of histidine, a homopolymer of lysine, a protein transduction domain, a protein transduction domain derived from an HIV-1 Tat protein, from a herpes simplex virus VP22 protein, or from a Drosophila antennapedia protein, a model protein transduction domain, or a model protein transduction domain comprising a homopolymer of D-arginine.

133. (Original) The composition of claim **131**, wherein the cellular delivery module is covalently attached to the RNA.

134. (Original) The composition of claim **133**, wherein the cellular delivery module is attached to the RNA through a disulfide bond, or wherein the covalent attachment is reversible by exposure to light of a preselected wavelength.

135. (Original) The composition of claim **133**, wherein the cellular delivery module comprises a lipid or one or more myristoyl groups.

136. (Original) The composition of claim **131**, wherein the cellular delivery module is associated with one or more second caging groups which inhibit the cellular delivery module from mediating introduction of the RNA into a cell.

137. (Original) The composition of claim **103**, wherein the RNA comprises a first polyribonucleotide comprising the sense strand and a second polyribonucleotide comprising the antisense strand, and wherein a cellular delivery module is covalently attached to the second polyribonucleotide.

138. (Original) The composition of claim **103** or **104**, wherein the first caging group is a cellular delivery module.

139. (Original) The composition of claim **103** or **104**, wherein the caged RNA is bound to a matrix.

140. (Original) The composition of claim 139, wherein the matrix is a surface, and the RNA is bound to the surface at a predetermined location within an array comprising other RNAs.

141. (Original) A kit for making the caged RNA of claim 103 or 104, comprising an RNA, one or more first caging groups, and instructions for assembling the RNA and the first caging groups to form the caged RNA, packaged in one or more containers; or comprising one or more first caging groups and instructions for assembling the first caging groups and an RNA supplied by a user of the kit to form the caged RNA, packaged in one or more containers.

142. (Original) A kit for making the caged RNA of claim 122 or 130, comprising one or more first caging groups, at least one label, and instructions for assembling the first caging groups, at least one label, and an RNA supplied by a user of the kit to form the caged RNA, packaged in one or more containers.

143. (Original) A method of selectively attenuating expression of a target gene in a cell, the method comprising:

introducing a caged RNA into the cell, the caged RNA comprising

(a) (i) an RNA comprising at least one double-stranded region, the double-stranded region comprising a sense strand and an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA corresponding to the target gene,

or

(ii) an RNA comprising a single polyribonucleotide strand comprising an antisense strand, the antisense strand comprising a region which is substantially complementary to a region of a target mRNA corresponding to the target gene,

and

(b) one or more caging groups associated with the RNA, the caging groups inhibiting the RNA from initiating RNA interference of the target mRNA in the cell; and,

initiating RNA interference of the target mRNA by exposing the cell to uncaging energy, whereby exposure to the uncaging energy frees the RNA from inhibition by the caging groups.

144. (Original) The method of claim **143**, wherein exposing the cell to uncaging energy comprises exposing the cell to light of a first wavelength.

145. (Original) The method of claim **144**, wherein exposing the cell to light of the first wavelength comprises exposing the cell to light wherein intensity of the light and duration of exposure of the cell to the light are controlled such that a first portion of the caged RNA is uncaged and a second portion of the caged RNA remains caged.

146. (Original) The method of claim **145**, comprising exposing the cell to light of the first wavelength again.

147. (Original) The method of claim **145**, wherein the first portion is a selected amount.

148. (Original) The method of claim **143**, comprising contacting the cell and a test compound, and wherein the cell is exposed to the uncaging energy at a preselected time point with respect to a time at which the cell and the test compound are contacted.

149. (Original) The method of claim **143**, wherein the uncaging energy is directed at a preselected subset of a cell composition comprising the cell.

150. (Original) The method of claim **143**, wherein the caged RNA comprises a cellular delivery module that can mediate introduction of the caged RNA into the cell, the cellular delivery module being associated with the RNA, and wherein introducing the caged RNA into the cell comprises contacting the cell with the caged RNA associated with the cellular delivery module.

151. (Original) The method of claim **143**, wherein the RNA comprises at least one label, the method comprising detecting a signal from the label.

152. -201. (Canceled).

202. (Original) A method of selectively attenuating expression of a target gene in a cell, the method comprising:

introducing a first caged DNA and a second caged DNA into the cell, the first caged DNA comprising a first DNA encoding an RNA sense strand and one or more caging groups associated with the first DNA, the second caged DNA comprising a second DNA encoding an RNA antisense strand and one or more caging groups associated with the second DNA,

the caging groups inhibiting transcription of the first and second DNAs, the first and second DNAs each comprising at least a portion of the target gene, and the sense and antisense strands being at least partially complementary and able to form a duplex over at least a portion of their lengths; and,

initiating RNA interference by generating double-stranded RNA by exposing the cell to uncaging energy, whereby exposure to the uncaging energy frees the first and second DNAs from inhibition by the caging groups and permits transcription of the first and second DNAs to occur.

203. (Original) The method of claim **202**, wherein the sense strand comprises a first polyribonucleotide and the antisense strand comprises a second polyribonucleotide, or wherein the sense and antisense strands comprise a single, self-complementary polyribonucleotide.

204. (Original) The method of claim **202**, wherein exposing the cell to uncaging energy comprises exposing the cell to light of a first wavelength.